IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	METZGER ET AL.	Examiner:	U. HO
Serial No.:	10/825,483	Group Art Unit:	3731
Filed:	April 14, 2004	Docket No.:	13033.5USC1
Title:	STIFFENING PHARYNGEAL WALL TREATMENT		

CERTIFICATE UNDER 37 CFR 1.8:
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, with sufficient postage, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on March 28, 2006.

By: Linda M. Beckman
Name: Linda M. Beckman

DECLARATION OF BRIAN J. ERICKSON
UNDER 37 C.F.R. §1.131

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

23552
PATENT TRADEMARK OFFICE

Brian J. Erickson declares as follows:

1. I am one of the co-inventors of the subject matter of above-referenced patent application which is a continuation application of U.S. Patent Application Ser. No. 10/237,149 filed September 6, 2002 as a continuation-in-part application of 10/066,967 filed February 4, 2002.
2. I submit this declaration as evidence that the invention disclosed and claimed in the '483 application was invented prior to August 13, 2002. More specifically, the invention of placing an implant in the pharyngeal airway with elasticity of the implant biasing the airway to patency was invented prior to August 13, 2002. Attached as Erickson Exhibit A (four pages) is a true and correct copy of a draft product requirement prepared at least by June 2002 for a project to place elongated struts in the pharyngeal wall to teat obstructive sleep apnea ("OSA"). At the time of the preparation of Erickson Exhibit A, I was Director of Research and Development at Restore Medical, Inc., assignee of the '483 application. My direct report, Anja Metzger, Ph.D., worked on this project at my

direction and prepared Erickson Exhibit A for this project. The preparation of Exhibit A was part of initial research and development activity that continued throughout 2002.

3. The foregoing statements are made of my own knowledge and are true. I hereby acknowledge I am warned that willful false statements and the like are punishable by fine or imprisonment, or both and may jeopardize the validity of the application or any patent issuing thereon (35 U.S.C. Sec. 25 and 18 U.S. C. Sec. 1001).

Dated: March 21, 2006 By: Brian J Erickson

Brian J Erickson

Pharyngeal Wall Support Device Requirements (DRAFT)

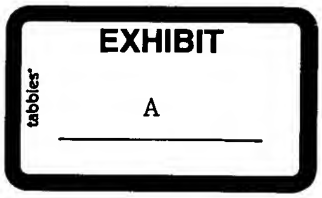
Summary of Operation: A device which has the ability to decrease the collapsibility, the compliance, or the air-flow resistance of the pharynx and/or acts to increase the cross-sectional area of the pharynx in an effort to modify the properties of the pharynx which contribute to obstructive sleep apnea.

Background: There are contrasting opinions in the medical literature on the mechanisms of OSA. OSA patients are a heterogeneous group; there are differing locations and patterns of pharyngeal collapse for each person. In addition to the physical findings and properties which characterize the pharynx in patients with OSA such as increased collapsibility, increased compliance, increased resistance, and decreased cross-sectional area, the physical properties and spatial relationships of the pharyngeal airway, head, and neck, as well as the neuromuscular integrity of the airway (reflexes affecting upper airway caliber) and mechanisms of breathing control (pharyngeal inspiratory muscle function) must also be considered relevant in their contribution to the mechanism and precipitation of upper airway collapse. (1, 2).

In general, obstructive apnea occurs during sleep, when the pharyngeal dilator muscle activity (genioglossus, tensor palatini, geniohyoid, stylohyoid) that normally maintains airway patency during inspiration through dilation of the airway, is diminished. (2, p. 85). When the intraluminal negative pressure of the airway reaches a critical point, the combination of redundant tissues and the loss of pharyngeal muscle tone causes airway collapse during inspiration. Please note, obstruction has been shown to occur during expiration and inspiration (8, 9); details on how upper airway area changes during the respiratory cycle can be found in the cited literature. Surgical treatments are aimed at eliminating any collapsible tissue in the airway and reducing airway resistance without creating functional impairment of the upper airway structures.

The multi-factorial mechanisms of obstructive sleep apnea pose an interesting design challenge; a device that addresses only one of the mechanisms of OSA may not be appropriate for all OSA patients, nor may it succeed if more than one mechanism is responsible for the OSA in a patient.

Functional Requirements of an OSA device:



Requirement:
1. Precise location of collapse must be identified on an individual by individual basis.

Rationale:
The location of pharyngeal collapse in a patient must first be identified so that the device can be targeted for the most appropriate location in the pharynx. It is important to identify the location of pharyngeal collapse so that a device is targeted for the precise location of the collapse. There is a consensus that the majority of airway collapse occurs in the retropalatal region, defined as the region from the level of the hard palate to the caudal tip of the soft palate (uvula) because the airway narrowing has been shown to be greatest in the retropalatal region (6). However, studies have also shown that collapse also occurs in the retroglossal region, defined from the caudal margin of the soft palate to the base of the epiglottis (1). A body of literature indicates that the lateral pharyngeal walls, rather than the anterior-posterior walls of the pharynx, are the structures which mediate the changes in upper airway size in OSA (6, 7, 9, 10).

a. Müller's maneuver with fiberoptic nasopharyngoscopy and cephalometric measurement are presently the key diagnostic tools used to identify the location of airway narrowing causing an apneic episode (2, p. 92). Fiberoptic endoscopy with or without the Müller maneuver has been shown to be able to effectively define the pattern and location of pharyngeal collapse in children (2, ref. #42, p. 29). However, contrasting literature claims that the Müller maneuver has not been demonstrated to accurately simulate an apneic event during sleep (6) and proposes that that a combination of MR imaging and nasopharyngoscopy with a Müller maneuver prior to UPPP may improve outcome after surgery. For example, if the

nasopharyngoscopy with Müller maneuver demonstrates retroglossal collapse and the MR imaging demonstrates primarily retroglossal narrowing, surgery directed at advancing the tongue such as geniohyoid advancement or maxillomandibular advancement should be considered rather than UPPP.

Requirement:

2. **The implant should affect the retropalatal lateral pharyngeal wall, by either preventing the thickening of these walls during sleep or the collapsibility of these walls.**

Rationale:

Does the airway collapse laterally or A-P? Posterior pharyngeal wall movement is observed in swallowing (11). Schwab has demonstrated that thickening of the lateral pharyngeal muscular walls is the major factor that leads to narrowing of the apneic retropalatal airway (10). The basis for the increased thickness of the lateral pharyngeal walls in apneics is unknown. Experiments utilizing HUPSEC (Hydrogen Ultrathin Phase-Encoded Spectroscopy) in conjunction with MR imaging indicate that the increased thickness of lateral pharyngeal wall in patients with sleep apnea is not secondary to increased fat infiltration or edema. Another plausible explanation for the thickening of the lateral walls is that weight gain results in increased muscle mass and an increase in the size of the lateral pharyngeal walls as well as the tongue and soft palate. Therefore, obesity may predispose to sleep apnea by theoretically increasing the size of the upper airway soft-tissue structures rather than by the direct deposition of fat in the parapharyngeal fat pads or by compressing the lateral airway walls by these fat pads. Studies have shown that the parapharyngeal fat pads do not compress the lateral airway walls in apneics (10). Apneics have thicker lateral pharyngeal walls when they are awake and these structures become even thicker during sleep (9). Studies have demonstrated a decrease in the electromyographic activity of the muscles of the lateral pharyngeal walls during sleep as well as the tensor palatini muscle of the soft palate (7, 14). The decrease in EMG activity may cause relaxation of these structures, contributing to the lateral wall thickening and airway narrowing. However, thickening of the lateral walls during sleep may be associated with state-related changes (asleep vs. awake) in the conformation of the soft palate and tongue. A complex three-dimensional biomechanical interaction may exist between the tongue, soft palate and lateral pharyngeal walls. The walls are a complex structure made up of a number of muscles including the hypoglossus, styloglossus, stylohyoid, stylopharyngeus, palatoglossus, palatopharyngeus, the pharyngeal constrictors, lymphoid tissue (palatine tonsils), and pharyngeal mucosa. The biomechanical relationships between these muscles and the way they interact with the soft palate and tongue are not well understood, nor is it understood how the lateral pharyngeal wall moves during respiration or during apnea to modulate airway size. Whether the airway actually collapses laterally or A-P is not discussed in the literature. MR anatomical studies demonstrate posterior movement and thickening of the soft palate with sleep as well as lateral pharyngeal wall thickening (7). Other studies have shown that increasing increment levels of effective CPAP therapy results in increased airway volume and area within the retropalatal and retroglossal regions, greater lateral than A-P airway dimensional changes, a decrease in the lateral pharyngeal wall thickness, and an increase in the distance between the lateral pharyngeal fat pads (9). Furthermore, effective mandible repositioning devices have been shown to thin the lateral pharyngeal walls; it is theorized that these devices may put traction on the lateral walls, resulting in the thinning of the walls. Subsequently, designing a device that affects the lateral pharyngeal walls seems appropriate in effectively addressing OSA. However, it is not clear, to this author, whether an implant should be implanted in the lateral walls or whether it should be positioned in the posterior wall.

Requirement:

3. **Implant shall withstand a transmural pressure differential of 8 cm H_2O (Patm – Pcrit).**

Rationale:

An effective device needs to be able to establish a pressure differential of 8 cm H_2O between nasal pressure and pharyngeal critical pressure (Pcrit) to eliminate obstructive sleep apnea **and** snoring. The

critical pressure is defined as the pressure that is equal to the pressures exerted on the airway by the surrounding tissue which is equal to the pressures tending to collapse the airway (3). It is determined by finding the level of nasal pressure below which maximal inspiratory airflow ceases (airway collapse)(5). A higher Pcrit equates to an increase in collapsibility. The Pcrit for normal people is < - 8 cm H_2O. For snorers the Pcrit is approximately - 4 cm H_2O, and for those with OSA, the Pcrit is approximately 0 cm H_2O. (3)

a. Device (or device in tissue) needs to be able to withstand a pressure of 4.4 cm H_2O to prevent collapse. This was the upper airway suction closing pressure found in OSA patients studies by Issa et al. (12)
b. Studies have shown that by sleeping with one's mouth open, a 4 cm H_2O increase in Pcrit can occur (3).
c. Effective UPPP surgery have demonstrated a reduction in Pcrit from –0.8 to –7.3 cm H_2O.(5)
d. Normal individuals maintain a positive pharyngeal transmural pressure of approximately 0 to 10 mm Hg (13.6 cm H_2O) during sleep. In contrast, upper airway obstruction in apneics is associated with development of negative transmural pressure during sleep. Clinically significant levels of obstructive sleep apnea can be produced when a nasal pressure of –10 cm H_2O is applied to normal subjects during sleep. These findings suggest that a disturbance in reflex responses is not necessary for the development of recurrent obstructive apneas (as some literature suggests). Rather, structural or neuromuscular factors that decrease the pharyngeal transmural pressure will predispose to this disorder (4).
e. Is it plausible that a small increase in the rigidity of the collapsible tissue is all that is necessary in order to prevent full collapse, i.e., any amount of stiffening will have the desired effect??

Requirement:

4. The device can not interfere with the mechanisms associated with swallowing, vocalization, and normal respiration.

Rationale:

We do not understand the dynamic biomechanical relationships between the upper airway muscles that allow physiologic functions like vocalization, swallowing, and respiration to occur. (6) Thus, it is difficult to predict how a device will impact these functions.

a. In the pharyngeal phase of swallowing, more than two dozen muscles are required to function together to effectively transport a bolus from the mouth to the esophagus. The posterior pharyngeal wall movement has been studied by Palmer et al., there is considerable mobility normally present in the posterior pharyngeal wall (retropalatal and retroglossal). (13) Will an implant interfere with the muscle activity, or will the muscle increase the chances of extrusion?

Requirement:

5. The device should be designed to be implantable in a typical apneic. The design shall be based on the following anatomical measurements (10):

a. thickness of lateral pharyngeal wall: (approx 30 mm)
b. anterior-posterior diameter of airway: (4.7 +/- 2.5 mm)
a. lateral diameter of airway (6.7 +/- 4.5 mm) at the level of the minimum airway area in apneics.

Requirement:

6. Anatomical structures in the pharyngeal region where the device should not be placed include:

a. the carotid arteries

Requirement:
7. The device, if implanted into the tissue, should be anchored to minimize chances of extrusion into the airway or into the surrounding structures.

Requirement:
8. Removability or reversibility of the device is desired.

Requirement:
9. Radiopacity - Efforts should be made to make prototypes radiopaque so that
   a. the device's position and influence on swallowing can be assessed,
   b. the device's effect on maintaining the airway patent at various inspiratory pressures can be visualized,
   c. the device is MR compatible.

Requirement:
10. The implant procedure should be less painful and less of a safety risk to the patient than comparable surgeries.

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* Recommended reading